Researchers' Guide to LTHT/UoL End of Trial Procedures

Scope: Describes the procedure all staff must follow when informing the relevant regulatory bodies of the end of a UoL/LTHT sponsored clinical trial.

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Original author: Daniel Skinner, QA Portfolio Coordinator
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Distribution & Storage:

Distribution to:

Investigators and all members of research teams conducting or assisting with a CTIMP sponsored by the University of Leeds or Leeds Teaching Hospital NHS Trust.

Location of document:

Paper: QA Department, Room 5, Research and Innovation Centre, St James' University Hospital
Electronic: [http://www.leedsth.nhs.uk/research/information-for-researchers/key-documents](http://www.leedsth.nhs.uk/research/information-for-researchers/key-documents)
   [http://ltthweb.leedsth.nhs.uk/sites/research-and-development/resources/Sponsored%20CTIMPs%20%28Quality%20Assurance%29](http://ltthweb.leedsth.nhs.uk/sites/research-and-development/resources/Sponsored%20CTIMPs%20%28Quality%20Assurance%29)

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Please note: This SOP should be used and followed in conjunction with other UoL / LTHT SOPs developed for researchers to support study set up and management. These can be found on the LTHT website or by contacting R&I / QA directly. For clinical trials where Leeds is not the trial Sponsor, please refer to any Sponsor SOPs for further information.

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Section A: Introduction

1.1 This Standard Operating Procedure (SOP) outlines the procedure for research teams to follow when a Clinical Trial of an Investigational Medicinal Product (CTIMP) Sponsored by either Leeds Teaching Hospitals NHS Trust (LTHT) or the University of Leeds (UoL) reaches its End of Trial Definition.

1.2 The definition of end of trial will be clearly defined in the study protocol. In most cases the definition will be the “Last participant, Last Visit” or “Last Participant, Last Data Item”.

1.3 Good practice is for protocols to specify a defined period following the last data collection point in the trial in order to allow for all subsequent data to be captured and sample analyses to take place.

1.4 It is the Chief Investigators (CI’s) responsibility to keep the Sponsor QA Office informed of any delays in reaching the end of trial definition.

1.5 When the end of trial definition is reached, the CI must notify:
   - The Sponsor Quality Assurance (QA) Office
   - The approving Research Ethics Committee (REC)
   - The Medicines for Healthcare products Regulatory Agency (MHRA)

1.6 The Chief Investigator or named delegate is also required to:
   - Make arrangements for the final research report (due within a year of the end of trial date, or 6 months for paediatric trials)
   - Make arrangements and notify the relevant bodies of the future use of the data collected in the trial
   - Fulfil commitments to study participants (if applicable), such as informing them of the outcomes of the trial and arrange archiving for the Trial Master File (TMF) and Investigator Site File (ISF).

Section B: Applicability

1.1 This SOP is applicable to all research staff involved in the trial management of single centre and multicentre UoL/LTHT Sponsored CTIMPs managed by a Clinical Trials Research Unit (excluding trials managed by the Leeds CTRU).
Section C: Researchers’ Guide to LTHT/UoL End of Trial Procedures

1. Notifying the Sponsor QA Office of the End of Trial.

1.1 Once the end of trial definition has been met, the CI and research team are required to complete and submit the “End of Trial Declaration Form”. The form must be completed by the Chief Investigator (or named delegate) using the template available on the MHRA website.

1.2 If the trial is being terminated early, a draft copy of the form must be sent to the Sponsor QA Office for information prior to submission to the REC and MHRA. This will be taken as the formal notification of early termination to the Sponsor, and the QA team will review the information on the form and flag any queries to the research team. Dependent on the information submitted, other further actions may also be requested by the Sponsor.

1.3 Copies of all forms and covering letters or emails submitted to the REC and MHRA must be forwarded to the QA office in real time and copies must also be stored in the Trial Master File/Investigator Site File.

1.4 The CI (or their delegate) is also responsible for notifying local NHS Trust (i.e. LTHT) and commercial services of the end of the trial. This should include NHS pharmacy services and where appropriate, other local services such as radiology and laboratories.

1.5 Two Months prior to the planned end of trial date (based on the original timelines specified within your IRAS application form), the Sponsor QA office will issue a reminder notifying the research team that the trial is due to end.

1.6 If the trial is not ending at this time, the Sponsor QA office will request justification as to why the trial end date has altered and request a new projected end date. Please note, Sponsor QA must be informed of any trial extensions in real time.

1.7 It is not possible to submit amendments to the trial once the ‘End of Trial Declaration Form’ has been submitted to the MHRA. All trial activities, including follow up visits, must therefore be completed before submission.

1.8 Should you wish to change the definition of end of trial wording within the protocol, this qualifies as an amendment to the Sponsor and Regulatory Bodies (Please see ‘QCRES_03研究人员 guide to Notification of Amendments for UoL LTHT Sponsored CTIMPs’ for further guidance).
2. Informing the REC of the End of Trial

2.1. The CI (or delegate) is responsible for notifying the REC once the end of trial is reached. The REC which originally gave a favourable opinion of the trial must be notified of its conclusion via email.

2.2. This email submission must include a copy of the End of Trial Declaration Form, and a cover letter notifying the REC in writing of the end of trial.

2.3. This form should be emailed to the REC within 90 days of the global end of trial (the date the trial ended in all countries) or within 15 days if the trial was terminated early.

2.4. There is no need to also inform the HRA of the end of a trial, as long as the REC committee who originally gave the favourable opinion is notified.

2.5. Please note that if the ‘End of Trial Declaration’ is submitted before the Annual Progress Report (APR) is due for submission, there is no need to submit an APR report to the REC covering this partial period. This information will instead be captured within the ‘End of Study Report’.

3. Informing the MHRA of the End of Trial

3.1 The CI (or delegate) is responsible for notifying the MHRA once the end of trial is reached. The MHRA must be notified of the trial’s conclusion via the Common European Submission Platform (CESP). Please contact the QA Office to arrange access to the CESP system.

3.2 The CESP submission must include a copy of the End of Trial Declaration Form (the same form used to inform the REC), and must be sent to the MHRA within 90 days of the global end of the trial (the date the trial ended in all countries), or within 15 days if the trial was terminated early.

3.3 Please note that if the ‘End of Trial Declaration’ is submitted before the Development Safety Update Report (DSUR) is due for submission, there is no need to submit a DSUR report to the MHRA covering this partial period. The information in this report will instead be captured within the ‘End of Study Report’.

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4. Submitting the Final Research Report to the MHRA

4.1. Within a year of the global end of trial date (For paediatric trials the reporting timeframe is reduced to 6 months), the CI (or delegate) is responsible for submitting a final research report, also referred to as the ‘End of Study Report’ to the MHRA via the EudraCT database.

4.2. For UoL and LTHT Sponsored trials the EudraCT upload is delegated to the Chief Investigator / Research Team or Clinical Trials Unit managing the trial.

4.3. It is good practice to start planning for the final analysis and report writing as soon as the end of trial form is submitted, not only to ensure the metric for completion is met, but also to reduce the impact on any other studies managed by your department.

4.4. Early submission of the end of trial report is encouraged. Do not wait until the absolute deadline date (1 year post end of trial) as the report can be submitted at any time within the year.

Accessing the EudraCT database and uploading results:

4.5. As trials are automatically registered on the EudraCT database when obtaining a EudraCT number during trial set-up, a record for your trial should already be in the system.

4.6. Immediately following submission of the End of Trial declaration form, the QA team will contact the research team, including the Chief Investigator of the trial, and the main trial contact/the member of staff who performed the statistical analysis for the trial as detailed in the protocol, via email detailing the requirements for submission to EudraCT and for updating all other trial registries the trial is registered on (ISRCTN, Clinicaltrials.gov etc.). This email will include instructions on signing up to the EudraCT system and accessing the individual trial record.

4.7. When the trial team has created an account on the system, the QA Portfolio Coordinator or delegate will then assign the trial to the research team using the account details obtained when the team register on the system. For further information on this process please contact the QA office.

4.8. The team will have a deadline of two weeks to arrange access to the system, request access to the trial record, and begin uploading information to the database. If this is not completed within this timeframe, a second reminder will be issued by the QA Portfolio Coordinator or delegate via email.

4.9. As 3 of the 6 sections on the system require updating by the individual who performed the statistical analysis for the trial, appropriate resource must be delegated by the CI to account for this at the onset of the task, to ensure that this does not lead to delays in the upload.

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4.10 After a period of 4 months from the date of the initial email (please see point 4.6), the QA team will contact the research team via email and request an update on progress, including an update on the status of the statistical analysis of the trial results. Any response received would be subject to a review by the QA team, and if there is no evidence of the task being underway, or if there are any delays in uploading results, this will be communicated to the relevant escalation point within the QA department.

4.11 After a period of 8 months from the date of the initial email (please see point 4.6), the QA team will again contact the research team via email and request an update on progress, including a request for confirmation that the results will be completed and posted on the system prior to the anniversary of the end of trial. If no response is received from the team, this will be escalated to the CSU Lead/LTHT Governance manager (for LTHT Sponsored CTIMPs)/Faculty Lead (for UoL Sponsored CTIMPs) for action.

4.12 Any response received to the email chase at 8 months will be subject to a review by the QA team, and if there is evidence that the task is not expected to be completed by the anniversary of the end of trial, this will be communicated to the relevant escalation point within the QA department if applicable.

4.13 When results are submitted to be posted on the system, the QA office must be notified prior to the results being submitted, so the record can be checked for completeness.

4.14 To notify the MHRA that results have been added to the system, the research team must send a confirmation email to ct.submission@mhra.gov.uk once the results information has been uploaded to EudraCT, with "End of trial: result related information: EudraCT XXXX-XXXXXXX-XX" as the subject line. You will not get an acknowledgement email or letter. A copy of this email and a copy of the end of trial report must be forwarded to the QA team in real time and copies of both must also be filed in the TMF.

4.15 If you have any issues with the upload, please contact the Sponsor QA office for assistance.

5. Submitting the Final Research Report to the REC

5.1 The CI (or delegate) is responsible for submitting a copy of the 'End of Trial Report' to the REC.

5.2 There is no standard format for final reports to the REC. A PDF copy of the EudraCT upload is sufficient.

5.3 A copy of the report must be submitted to the approving REC via email, with the Trial name and REC reference clearly marked in the subject line. A copy of the email must then be forwarded onto the QA team for confirmation purposes.

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6. Early Termination of a CTIMP

Decision to terminate the trial made by the Chief Investigator / Trial Steering Committee (TSC)

6.1 When a decision is made by the Chief Investigator to terminate a CTIMP early - either as a result of a TSC/DMEC meeting or as a result of notification from the relevant regulatory bodies (REC/MHRA) it is the responsibility of the CI (or their delegate) to notify the Sponsor QA office. This notification should be in writing as soon as the decision is made.

6.2 Details of the termination should be captured on a Declaration of End of Trial form, and sent to the Sponsor QA Office prior to submission to the REC and MHRA. This will be taken as the formal notification of early termination to the Sponsor, and the QA team will review the information on the form and flag any queries to the research team. The CI is then responsible for submitting this to the Competent Authority (MHRA via CESP) and REC within 15 days of the date of suspension or termination, along with a covering letter identifying:

- Protocol number
- EudraCT number
- Explanation of the reasons for terminating the trial
- Any related documentation (once available)

Decision to terminate the trial made by the Competent Authority (MHRA) or REC

6.3 Where a decision to prematurely terminate a CTIMP comes from the MHRA or REC via the Sponsor QA Office, a member of the QA team will notify the CI within a maximum of three working days of the Sponsor receiving the notification.

6.4 The CI must terminate the trial using the same process as described in Section 6.1, after discussing the treatment implications for any patients still participating in the trial.

Decision to terminate the trial made by the Sponsor office:

6.5 Where a decision to prematurely terminate a CTIMP comes from the Sponsor, for example as a result of a critical finding identified during a monitoring visit, the Sponsor QA Office is responsible for:

Notifying the CI of:

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The reasons why the CTIMP is being suspended or terminated early.

The date that suspension or termination will begin and;

Any corrective action that they are required to take.

Notifying all other Principal Investigators (via the CI or their delegate) of:

The date that suspension or termination of the trial will begin and;

Any local action that they are required to take.

6.6 Although the sponsor QA team have made the decision to terminate the trial, the CI is responsible for notifying the REC and MHRA of termination, and submitting the End of trial declaration form via email and CESP.

6.7 Also, although the trial has been terminated early, if participants have been recruited to the trial and data has been collected from participants, the CI/Research team has a responsibility to report this data through EudraCT, with the trial clearly marked as ‘terminated early’ on the system. For further information on this process please contact the QA office.

Section D: References

MHRA Good Clinical Practice Guide 2012
EudraCT Results Database & Training/Guidance - [https://eudract.ema.europa.eu/training.html](https://eudract.ema.europa.eu/training.html)
CESP Portal- [https://cespportal.hma.eu/Account/Login?ReturnUrl=%2f](https://cespportal.hma.eu/Account/Login?ReturnUrl=%2f)

Section E: Acronyms & Glossary

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<td>CTIMP</td>
<td>Clinical Trial of an Investigational Medicinal Product</td>
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<td>Development Safety Update Report</td>
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